



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/541,033	03/31/2000	Richard G. Miller	35828-0079	3667

21839 7590 04/04/2003

BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER

ROARK, JESSICA H

ART UNIT	PAPER NUMBER
----------	--------------

1644

DATE MAILED: 04/04/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/541,033

Applicant(s)

MILLER ET AL.

Examiner

Jessica H. Roark

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2003 and 11 March 2003 and 17 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 January 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>25</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1644

DETAILED ACTION

1. Applicant's Brief on Appeal, filed 1/31/03 (Paper No. 22), is acknowledged.
2. Upon further consideration of the issue raised in the attached Interview Summary (Paper No. 25, 3/11/03) and commented upon in Applicant's Communication of 3/17/03 (Paper No. 26); the finality of the last Office action is withdrawn. A non-final Office Action on the merits follows.
3. Claims 1-11 are pending.
4. Applicant's species election without traverse in Paper No. 8 (filed 3/1/01) of a method of treating a mammalian subject suffering from the autoimmune disease rheumatoid arthritis by administering autologous mammalian blood that has been modified extracorporeally by a combination of the stressors which are an oxidative environment, electromagnetic emission and a temperature above body temperature, in combination with a therapeutic treatment that comprises administration of a tumor necrosis factor inhibitor that is the recombinant TNF receptor p75 TNFR:Fc is again acknowledged.

Drawings

5. The drawings submitted 1/31/03 have been approved by the Draftsman.

Priority

6. Provisional application 60/127,621, filed April 1, 1999, appears to provide adequate written support for the instant claims.

Specification

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed*.

The following title is suggested:

-- COMBINATION THERAPY USING MODIFIED AUTOLOGOUS BLOOD FOR TREATMENT OF RHEUMATOID ARTHRITIS -- .

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

Art Unit: 1644

Claim Rejections – 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bolton (US Pat. No. 5,980,954, IDS) and Jacobs et al (US Pat. No. 5,605,690, of record).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention “by another”; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The claims are drawn in view of an election of species to a method of treating a subject suffering from rheumatoid arthritis by administering the therapeutic treatment of p75 TNFR:Fc and autologous blood exposed to an oxidative environment, electromagnetic emission, and a temperature above body temperature.

Bolton teaches and claims a method of treating a subject suffering from rheumatoid arthritis by administering autologous blood exposed to an oxidative environment, electromagnetic emission (i.e., UV radiation), and a temperature above body temperature (see entire document, especially claims and Abstract). Electromagnetic emission is taught via a specific embodiment, UV radiation (e.g., claim 6-7 and column 8). Bolton also teaches that this method can be generally applied to a variety of autoimmune and inflammatory conditions, specifically including multiple sclerosis, scleroderma, diabetes, inflammatory bowel disease, psoriasis, atherosclerosis, and organ rejection (see especially column 9 at lines 29-40).

The Examiner acknowledges that Bolton does not teach co-administration of a therapeutic treatment that is a TNF inhibitor, including p75 TNFR:Fc.

Art Unit: 1644

However, Jacobs et al. teach and claim a method of lowering the levels of active TNF- α in a mammal having arthritis by administering a TNF antagonist, including TNFR:Fc (see entire document, especially claims and Examples 4-6). Jacobs et al. further teach the specific therapeutic treatment comprising TNFR:Fc p75 (e.g., Examples 1 and 2 in conjunction with columns 2-3 "Definitions").

Jacobs et al. further teach that a combination therapy of TNFR:Fc and another composition that also mediates a partial reduction in arthritis symptoms (rmu IL-1R) resulted in greater reduction of arthritis symptoms than did administration of either composition alone, i.e., Jacobs et al. observed synergy when individual treatments were combined (see especially Example 4 at columns 17-18).

Thus the ordinary artisan at the time the invention was made would have found it obvious to modify the invention taught by Bolton for the treatment of rheumatoid arthritis by combining it with the teachings of Jacobs et al.

Given the teachings of Bolton that modified autologous blood could be used to treat rheumatoid arthritis and the teachings of Jacobs et al. that combining additional treatments for rheumatoid arthritis with TNFR:Fc resulted in a synergistic therapy; it would have been obvious to the ordinary artisan at the time the invention was made that the treatment taught by Bolton could be combined with the treatment of Jacobs et al. to result in a treatment of rheumatoid arthritis that would be more effective than either treatment used alone.

The teachings of Jacobs et al. that combination therapy involving TNFR:Fc was advantageous for the treatment of rheumatoid arthritis would have motivated the ordinary artisan at the time the invention was made to combine the modified autologous blood treatment taught by Bolton with the TNFR:Fc treatment taught by Jacobs et al. to provide a more efficacious treatment of rheumatoid arthritis using such a combination therapy.

Given that each treatment of rheumatoid arthritis worked individually, the ordinary artisan would have had a reasonable expectation of success with respect to the combination therapy. Further, given the teachings of Jacobs et al. that combining other treatments of rheumatoid arthritis with TNFR:Fc provided a synergistic treatment, the ordinary artisan at the time the invention was made would have had a reasonable expectation that addition of the modified autologous blood therapy to the TNFR:Fc therapy of Jacobs et al. would result in not only an additive effect, but even a synergistic effect.

Applicant is reminded that it is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. In *re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Further, the ordinary artisan at the time the invention was made would have recognized that the therapeutic treatment (i.e., TNFR:Fc) and modified blood could have been administered either simultaneously or consecutively while still functioning as a synergistic combination. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's comment in the Communication filed 3/17/03 regarding a possible obligation of assignment is acknowledged.

However, until such time as a statement is provided for the record that meets the requirements set forth *supra* with respect to what appears to be a common assignee between the instant application and U.S. Pat. No. 5,980,954 to Bolton; the instant rejection appears to be appropriate.

Art Unit: 1644

11. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bolton (US Pat. No. 5,591,457) and Jacobs et al (US Pat. No. 5,605,690, of record).

The claims are drawn in view of an election of species to a method of treating a subject suffering from rheumatoid arthritis by administering the therapeutic treatment of p75 TNFR:Fc and autologous blood exposed to an oxidative environment, electromagnetic emission, and a temperature above body temperature.

Bolton teaches a method of treating a subject suffering from rheumatoid arthritis by administering autologous blood exposed to an oxidative environment, electromagnetic emission (i.e., UV radiation), and a temperature above body temperature (see entire document, especially column 7 in view of columns 4-5). Electromagnetic emission is taught via a specific embodiment, UV radiation (e.g., column 7 at line 21). Bolton et al. also teach that this method can be generally applied to a variety of autoimmune and inflammatory conditions, specifically including multiple sclerosis, systemic lupus erythematosus, diabetes, inflammatory bowel disease, psoriasis, graft-versus-host disease and organ rejection (see especially column 7 at lines 28-53).

Bolton teaches that the modified autologous blood activates the human immune system by stimulating T lymphocytes and monocytes and increasing their potential to proliferate (see e.g. column 3, especially lines 44-55). Bolton teaches at column 17 (see especially lines 15-41) that the modified autologous blood stimulates these cells to proliferate when the cells are contacted with a combination of the modified blood and the cytokine IL-2.

The Examiner acknowledges that Bolton does not teach co-administration of a therapeutic treatment that is a TNF inhibitor, including p75 TNFR:Fc.

However, Jacobs et al. teach and claim a method of lowering the levels of active TNF- α in a mammal having arthritis by administering a TNF antagonist, including TNFR:Fc (see entire document, especially claims and Examples 4-6). Jacobs et al. further teach the specific therapeutic treatment comprising TNFR:Fc p75 (e.g., Examples 1 and 2 in conjunction with columns 2-3 "Definitions").

Jacobs et al. further teach that a combination therapy of TNFR:Fc and another composition that also mediates a partial reduction in arthritis symptoms (rmu IL-1R) resulted in greater reduction of arthritis symptoms than did administration of either composition alone, i.e., Jacobs et al. observed synergy when individual treatments were combined (see especially Example 4 at columns 17-18).

Thus the ordinary artisan at the time the invention was made would have found it obvious to modify the invention taught by Bolton for the treatment of rheumatoid arthritis by combining it with the teachings of Jacobs et al.

Given the teachings of Bolton that modified autologous blood could be used to treat rheumatoid arthritis and the teachings of Jacobs et al. that combining additional treatments for rheumatoid arthritis with TNFR:Fc resulted in a synergistic therapy; it would have been obvious to the ordinary artisan at the time the invention was made that the treatment taught by Bolton could be combined with the treatment of Jacobs et al. to result in a treatment of rheumatoid arthritis that would be more effective than either treatment used alone.

The teachings of Jacobs et al. that combination therapy involving TNFR:Fc was advantageous for the treatment of rheumatoid arthritis would have motivated the ordinary artisan at the time the invention was made to combine the modified autologous blood treatment taught by Bolton with the TNFR:Fc treatment taught by Jacobs et al. to provide a more efficacious treatment of rheumatoid arthritis using such a combination therapy.

Art Unit: 1644

Given that each treatment of rheumatoid arthritis worked individually, the ordinary artisan would have had a reasonable expectation of success with respect to the combination therapy. Further, given the teachings of Jacobs et al. that combining other treatments of rheumatoid arthritis with TNFR:Fc provided a synergistic treatment, the ordinary artisan at the time the invention was made would have had a reasonable expectation that addition of the modified autologous blood therapy to the TNFR:Fc therapy of Jacobs et al. would result in not only an additive effect, but even a synergistic effect.

Applicant is reminded that it is prima facie obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. In *re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Further, the ordinary artisan at the time the invention was made would have recognized that the therapeutic treatment (i.e., TNFR:Fc) and modified blood could have been administered either simultaneously or consecutively while still functioning as a synergistic combination. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,980,954 (of record) in view of Jacobs et al (US Pat. No. 5,605,690, of record). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The claims are drawn in view of an election of species to a method of treating a subject suffering from rheumatoid arthritis by administering the therapeutic treatment of p75 TNFR:Fc and autologous blood exposed to an oxidative environment, electromagnetic emission, and a temperature above body temperature.

Art Unit: 1644

U.S. Pat. No. 5,980,954 claims a process of treating a mammalian patient suffering from an autoimmune disease (claim 1), including rheumatoid arthritis (claim 10) by administering autologous blood that has been modified by ozone gas (i.e., an oxidative environment), ultraviolet radiation (i.e., electromagnetic emission) and a temperature above body temperature (see especially claims 1 and 4).

U.S. Pat. No. 5,980,954 does not claim co-administration of a therapeutic treatment that is the TNF inhibitor, including p75 TNFR:Fc.

However, Jacobs et al. teach and claim a method of lowering the levels of active TNF- α in a mammal having arthritis by administering a TNF antagonist, including TNFR:Fc (see entire document, especially claims and Examples 4-6). Jacobs et al. further teach the specific therapeutic treatment comprising TNFR:Fc p75 (e.g., Examples 1 and 2 in conjunction with columns 2-3 "Definitions").

Jacobs et al. further teach that a combination therapy of TNFR:Fc and another composition that also mediates a partial reduction in arthritis symptoms (rmu IL-1R) resulted in greater reduction of arthritis symptoms than did administration of either composition alone, i.e., Jacobs et al. observed synergy when individual treatments were combined (see especially Example 4 at columns 17-18).

Thus the ordinary artisan at the time the invention was made would have found it obvious to modify the invention claimed in U.S. Pat. No. 5,980,954 for the treatment of rheumatoid arthritis by combining it with the teachings of Jacobs et al.

Given the invention claimed in U.S. Pat. No. 5,980,954 and the teachings of Jacobs et al. that combining additional treatments for rheumatoid arthritis with TNFR:Fc resulted in a synergistic therapy; it would have been obvious to the ordinary artisan at the time the invention was made that the treatment claimed in U.S. Pat. No. 5,980,954 could be combined with the treatment of Jacobs et al. to result in a treatment of rheumatoid arthritis that would be more effective than either treatment used alone.

The teachings of Jacobs et al. that combination therapy involving TNFR:Fc was advantageous for the treatment of rheumatoid arthritis would have motivated the ordinary artisan at the time the invention was made to combine the modified autologous blood treatment claimed in U.S. Pat. No. 5,980,954 with the TNFR:Fc treatment taught by Jacobs et al. to provide a more efficacious treatment of rheumatoid arthritis using such a combination therapy.

Given that each treatment of rheumatoid arthritis worked individually, the ordinary artisan would have had a reasonable expectation of success with respect to the combination therapy. Further, given the teachings of Jacobs et al. that combining other treatments of rheumatoid arthritis with TNFR:Fc provided a synergistic treatment, the ordinary artisan at the time the invention was made would have had a reasonable expectation that addition of the modified autologous blood therapy to the TNFR:Fc therapy of Jacobs et al. would result in not only an additive effect, but even a synergistic effect.

Applicant is reminded that it is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06.

Further, the ordinary artisan at the time the invention was made would have recognized that the therapeutic treatment (i.e., TNFR:Fc) and modified blood could have been administered either simultaneously or consecutively while still functioning as a synergistic combination. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Art Unit: 1644

14. Claims 1-11 are directed to an invention not patentably distinct from claims 1-12 of commonly assigned U.S. Patent No. 5,980,954 (of record) for the reasons set forth supra.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 5,980,954, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

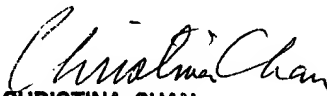
Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
April 2, 2003


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600